

## REMARKS

In the Final Office Action dated May 23, 2007, claims 1-24 are pending and are under consideration. Claims 1-24 are rejected as allegedly obvious over U.S. Patent No. 4,675,296 to Lehmussaari et al. ("the '296 patent") in view of Marinchenko et al. (*Appl. Biochem. Microbiol.* 15(6): 670-73 (1979)) ("Marinchenko").

Applicant has amended Claim 1 by reciting that the cereal is ungerminated. Support for the term "ungerminated" is found on the bottom of page 4 of the specification. Applicant has also amended Claim 1 by incorporating the subject matter of Claims 2 and 16 into Claim 1, accordingly, applicants have cancelled Claims 2 and 16. Claim 3 is amended to depend from Claim 1 in view of the cancellation of Claim 2. Applicant further amends Claim 1 to delineate that the recovering of the  $\beta$ -amylase from the medium is "in purified form" and adds a dependent Claim 27 to delineate the recovering of the  $\beta$ -amylase from the medium "in purified and concentrated form." The support for the recitation "in purified form" and "in purified and concentrated form" can be found in paragraphs 19, 30 and 48 of the instant specification. Moreover, Applicant adds Claims 25-26, which depend from Claim 1, to further delineate the yield of  $\beta$ -amylase obtainable from the cereal. Support for Claim 25-26 is found in paragraph 21 and Examples 5-6 of the specification. With respect to Claim 26, it is to be noted that the text in paragraph 21 provides that when cellulase is added to the extraction water, as much as 65% of the total amount of  $\beta$ -amylase can be extracted. However, as further described in paragraph 21, in the prior art, which does not utilize cellulase, the extraction yield is 45 to 50% of the total  $\beta$ -amylase. Thus, the use of cellulase increases the yield between 10 to 15% units higher. Furthermore, Examples 5 and 6 show increased yields from 39.4 to 56.7% and from 11.5% to 25.3% when cellulase is utilized, which is about 10-15% higher. This provides implicit support

for the subject matter in Claim 26. See, In re Robins, 429 F.2d 452, 456-457, 166 USPQ 552, 555 (CCPA 1970). Furthermore, Claim 28 is added to further delineate the subject matter of Claim 1 to a process of extracting  $\beta$ -amylase from barley and Claim 29 is added, which depends from Claim 28, to delineate the yield of extracted  $\beta$ -amylase from barley. Support for Claim 28 is found in previously presented Claim 1 and in paragraphs 16 and 19 of the specification. Support for Claim 29 is found in paragraph 21 of the specification.

No new matter is introduced by the amendment to Claims 1 and 3 or the addition of Claims 21-29.

This Response addresses the Examiner's only rejection. Applicant therefore respectfully submits that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

The Examiner has maintained the rejection of Claims 1-24 as allegedly obvious over U.S. Patent No. 4,675,296 to Lehmussaari et al. ("the '296 patent") in view of Marinchenko et al. (*Appl. Biochem. Microbiol.* 15(6): 670-73 (1979)).

Applicant respectfully submit that the '296 patent is directed to a process for preparing a commercial  $\beta$ -amylase product from whole or at least partially dehusked barley grain by extracting the grain with water, which may contain a reducing agent. As described in column 2, lines 30-40 of the '296 patent, the grain surfaces in the barley grain act as a semi-permeable filter, allowing the  $\beta$ -amylase and some low molecular weight substances to pass into the water. In other words, the '296 patent teaches that the grain's surface should be kept intact to maintain the grain surface so that it can act as a filter. Moreover, the '296 patent does not utilize cellulase to extract  $\beta$ -amylase from the barley grain. A review of the '296 patent clearly reveals that the

'296 patent does not teach, disclose or suggest or even recite the use of cellulase in its process for preparing the  $\beta$ -amylase product, a position with which the Examiner agrees.

On the other hand, the present invention recognizes that the use of the enzyme cellulase in a process of extracting  $\beta$ -amylase from cereal grains surprisingly improves the yield of  $\beta$ -amylase and reduces the extraction time. The cereal grains in the present invention can be unhusked, dehusked, milled, ground or polished grains. In contrast to the present invention, the '296 patent specifically teaches that the grain surface layer underneath the husk should be kept intact so that the surface layer can function as a filter to obtain a  $\beta$ -amylase with minor impurities. Since cellulase breaks down the surface structures underneath any husk of a living grain, the use of cellulase in extracting  $\beta$ -amylase from cereal grains, as presently claimed, would contradict the teaching in the '296 patent. In other words, the '296 patent actually teaches away from the use of cellulase, as in the present invention.

In the Final Office Action, the Examiner alleges that the '296 patent discloses extracting  $\beta$ -amylase from ground or otherwise degraded material, such as barley flour. The Examiner refers to Example I of the '296 patent.

However, Applicant observes that the '296 patent obtains a  $\beta$ -amylase extract from whole or partially dehusked grains utilizing only reducing agents which, according to the '296 patent, convert based  $\beta$ -amylase to free amylase without the use of "arduous purification" steps post extraction and without breaking the grain surface. Inasmuch as cellulase breaks down the surface structure underneath any husk of a living grain, (see page 6, lines 9-16 of the instant application), the '296 patent would not utilize cellulase and actually teaches away from the use of cellulase as it breaks the grain's surface. As acknowledged in the '296 patent, the prior art has already disclosed the use of ground or crushed grains for extracting  $\beta$ -amylase.

Example I of the '296 patent merely demonstrates that the use of whole or dehusked barley (without breaking grain surface) can yield 35% of extractable  $\beta$ -amylase, and at the same time the  $\beta$ -amylase extract prepared from whole or dehusked barley contains fewer other grain ingredients than the  $\beta$ -amylase extract prepared from ground and crushed grains.

Thus, Applicant respectfully submits that based on the teaching of the '296 patent, adding cellulase to the barley used in the '296 patent, including the dehusked barley, would break the grain surface structures underneath the husk, thereby destroying the use of the grain surface layers to act as a filter and block other grain ingredients from mixing with the  $\beta$ -amylase extract, as required in the '296 patent. Thus, Applicant respectfully submits that the '296 patent would not have provided any motivation to those skilled in the art to consider using cellulase in the process.

The Examiner has alleged in the Final Action that the secondary reference to Marinchenko provides the motivation to use cellulase. The Examiner contends that Marinchenko teaches an increase in net amylolytic activity by freeing amylases. The Examiner contends that by referencing amylases in the plural, Marinchenko teaches using cellulase to treat barley materials to increase both  $\alpha$  and  $\beta$  amylases. The Examiner alleges that the likelihood that  $\beta$ -amylase would also be increased is not excluded.

Marinchenko teaches enhancing amylolytic activities in malt for saccharification of starch used in the brewing industry. It is not used to remove  $\beta$ -amylase from cereal, as in the present application. Thus, Marinchenko is directed to a totally different field of use as the '296 patent and there is no reason to combine its teaching with the '296 patent in the first instance. Moreover, the '296 patent teaches away from combining it with Marinchenko. As indicated hereinabove, the '296 patent teaches that the grain surface layer underneath the husk should be

kept intact so that the surface layers can function as a filter. Thus, it teaches away from the use of a substance that breaks down the surface structure, such as cellulase. Accordingly, since Marinchenko utilizes cellulase, the '296 patent teaches away from combining it with Marinchenko.

Moreover, Applicant respectfully submits that Marinchenko does not distinguish between  $\alpha$  and  $\beta$  amylases. It is respectfully submitted that free  $\alpha$  amylase, rather than  $\beta$  amylase, is responsible for the increased activities observed by Marinchenko. In this connection, Applicant respectfully submits an illustration of a mature cereal grain. See Exhibit A. As shown in Exhibit A,  $\alpha$  amylase and  $\beta$  amylase are located in totally different parts of the grain in cereal (such as barley and wheat). As further illustrated and described by Exhibit D (*Enzymers and Their Role in Cereal Technology* by J.E. Kruger et al., American Association of Cereal Chemists, Inc., St. Paul, Minnesota, 1987), particularly on pages 97 and 122,  $\alpha$  amylase is located in the outer layers, mostly in the pericarp and small amounts are present in the aleurone. In contrast, as further illustrated and described by Exhibit B (*Wheat Chemistry and Technology* by Y. Pomeranz, American Association of Cereal Chemists, Inc., St. Paul, Minnesota, 1978), particularly, on page 462, all the  $\beta$  amylase is located in the inner parts of the grain in the starchy endosperm. Applicant also submits Exhibit C (*Cereal Science and Technology* by G.H. Palmer, Aberdeen University Press, 1989) for clarification of the physical form of the pericarp, aleurone and endosperm. See, e.g., page 102 of Exhibit C.

Applicant respectfully submits that in the malting process, the amount of  $\alpha$  amylase increases significantly (100-1000 times) in the outer (pericarp) layer. In the brewing of malt, the objective is to have as much  $\alpha$  amylase available to degrade starch. Therefore, it is advantageous in the malting process to use cellulase to increase the total amount of  $\alpha$  amylase by

releasing it from the hemicellulase-cellulase matrix of the pericarp of the cell wall. Marinchenko specifically points out that "the content of free amylases should be promoted by enzymes degrading cell walls." See the Abstract of the Marinchenko reference. Applicant respectfully submits that this statement by Marinchenko clearly refers to  $\alpha$  amylase which is present in the cell walls. As mentioned above,  $\beta$  amylase is located in the central starchy endosperm part of the grain and not in the cell walls. Applicant also respectfully submits that in contrast to the Examiner's allegation, it is well known in the art, such as the teaching in Exhibits A-D, that  $\beta$ -amylase is not enhanced in the malting process.

Additionally, Applicant respectfully submits that in a brewing or malting process such as the one described by Marinchenko, it would not be considered advantageous to use cellulase to release  $\beta$  amylase so that it would be more easily available, because  $\beta$ -amylase is not located in the hemicellulase-cellulase matrix of the cell wall at all. Marinchenko uses cellulase to a free  $\alpha$  amylase from the cell walls and Marinchenko's target of the cell wall is totally different from the one in the present invention, i.e. the grain surface. In contrast, the present invention is focused on extracting  $\beta$ -amylase located in the central endosperm of the grains and not in the cell walls. Thus in contrast to the allegations by the Office Action, Marinchenko does not relate to the extracting of  $\beta$ -amylase from a cereal grain.

Moreover, in contrast to the teaching of Marinchenko, the present invention uses ungerminated grains (see bottom of page 4 of the specification) in which the amount of  $\alpha$  amylase is much lower compared to the  $\alpha$  amylase content in the malted grains used by Marinchenko. Applicant submits that there is indeed a great difference between malted grains such as those used by Marinchenko and ungerminated grains such as those used in the present

invention. Thus, Marinchenko does not teach, disclose or suggest the use of ungerminated grains.

In summary, it is respectfully submitted that there is no motivation to combine Marinchenko with the '296 patent in the first instance as the '296 patent teaches away from the use of a substance, like cellulase, that breaks the grain surface. Moreover, the teachings of Marinchenko relate to the use of malt for saccharification of starch for use in the brewing industry. Thus the process disclosed in Marinchenko is totally unrelated to the process described in the '296 patent.

Further, the '296 patent in combination with Marinchenko does not teach or suggest a method for extracting  $\beta$ -amylase from ungerminated cereal, as claimed using cellulase. The '296 patent does not utilize cellulase to obtain  $\beta$ -amylase. The '296 patent utilizes just water and optionally reducing agents in the absence of cellulase. Marinchenko, on the other hand, utilizes cellulase to remove  $\alpha$ -amylase without enhancing  $\beta$ -amylase. Thus the combination of the primary and secondary reference do not teach, disclose or suggest the use of cellulase in extracting  $\beta$ -amylase from ungerminated cereal.

Applicant respectfully submits that the secondary reference to Marinchenko does not ameliorate the deficiencies of the primary reference to the '296 patent. The combination of the '296 patent and Marinchenko does not teach the use of cellulase for extracting  $\beta$ -amylase from ungerminated cereal as claimed. Therefore, in view of the foregoing arguments and the amendments to the claims, Applicant respectfully submits that the present invention is not obvious in view of the cited references.

Furthermore, Applicant observes that in the Advisory Action, the Examiner appears to confuse the grain structures of husk/hull with grain surface. For example, the

Examiner alleges that the '296 patent teaches the use of a "permeable hull." Applicant respectfully submits that the '296 patent requires an intact "permeable grain surface", while the hull or husk or the grain can stay or can be removed. In addition, the Examiner still alleges in the Advisory Action that the '296 patent motivates the extraction of  $\beta$ -amylase using ground or otherwise degraded material, such as barley flour. In this regard, Applicant respectfully submits that the Examiner has misinterpreted the disclosure of the '296 patent. The Examiner in the Final Action alleged the same by referring to Example I of the '296 patent. Applicant respectfully directs the Examiner's attention to the section entitled "SUMMARY OF THE INVENTION," in the '296 patent which explicitly teaches that "[t]he invention provides for a process for extracting  $\beta$ -amylase which comprises steeping whole or at least partially dehusked barley grain in water . . . wherein the grain surface layers act as a semipermeable filter, thereby allowing the enzyme to pass into the water, but retaining other grain ingredients." In the section entitled "BEST MODE FOR CARRYING OUT THE INVENTION," the '296 patent teaches that "[i]n accordance with the present invention, it has been found that  $\beta$ -amylase can be extracted by water from whole or at least partially dehusked barley grain without any prior crushing or grinding of the grain." Emphasis added.

Thus, Applicant respectfully submits that the '296 patent obtains a  $\beta$ -amylase extract from whole or partially dehusked grains utilizing reducing agents, which convert based  $\beta$ -amylase to free amylase without the use of "arduous purification" steps post extraction and without breaking the grain surface. Since cellulase breaks down the surface structure underneath any husk of a living grain, in view of the '296 patent, one would not be motivated to use cellulase. Applicant respectfully submits that Example I of the '296 patent merely demonstrates that the use of whole or dehusked barley (without breaking grain surface) can yield 35% of

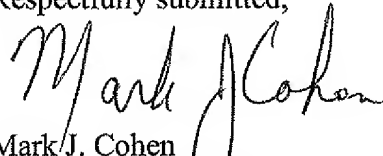


extractable  $\beta$ -amylase, while, at the same time, the  $\beta$ -amylase extract prepared from whole or dehusked barley contains fewer other grain ingredients than the  $\beta$ -amylase extract prepared from ground and crushed grains. The '296 patent acknowledges in the section entitled "BACKGROUND OF THE INVENTION" that the prior art has already disclosed the use of ground or crushed grains for extracting  $\beta$ -amylase. Indeed, the objective of the '296 patent appears to overcome the disadvantage of the method in the prior art.

In view of the foregoing and further in view of the amendment to Claims 1 and 3, the rejection of Claims 1-24 as allegedly obvious over U.S. Patent No. 4,675,296 to Lehmussaari et al. in view of Marinchenko et al. is overcome, and withdrawal thereof is respectfully requested. Applicant further submits that the newly added Claims 21-29 are not obvious in view of the cited art and the Applicant's foregoing argument.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Encls.: Exhibits A-D